

REMARKS

Claims 109-121, as amended, and new claims 122-123 are presented herein for the Examiner's review and consideration. Claim 109 has been amended to recite a preferred embodiment, wherein the method comprises binding a first label to at least one ribosome or a fragment thereof to form a donor fluorophore; binding a second label to at least one tRNA to form an acceptor fluorophore; detecting electromagnetic radiation signals emitted when the first and second labels are in proximity, wherein the signals are obtained from the donor and acceptor fluorophores forming a fluorescence resonance energy transfer (FRET) pair, with the signals indicating progression of the synthesis of the one or more proteins; and analyzing the detected signals to identify one or more proteins being synthesized by producing a FRET signal from the FRET pair, computing a synthesis signal from the FRET signal, and interrogating a database compiled from signal data of various FRET pairs so as to identify the one or more proteins that most likely have produced the detected signals. Support for this change is found in the specification in paragraph [0029] and in the section entitled Fluorescent Resonance Energy Transfer (FRET) starting at paragraph [0086] as well as in the Abstract of the published specification. Claim 111 has been amended to be consistent with claim 109. Also, new claims 122-123 have been added. These claims are supported by the specification in paragraph [248] of the published US application. As no new matter has been introduced by these changes and additions, they all should be entered at this time.

Claims 109-121 have been rejected under 35 U.S.C. 112, second paragraph, for the reasons set forth on page 3 of the office action. In response, claim 109 has been amended to make it clear that the method comprises binding a first label to at least one ribosome or a fragment thereof to form a donor fluorophore; binding a second label to at least one tRNA to form an acceptor fluorophore; detecting electromagnetic radiation signals emitted when the first and second labels are in proximity, wherein the signals are obtained from the donor and acceptor fluorophores forming a fluorescence resonance energy transfer (FRET) pair, with the signals indicating progression of the synthesis of the one or more proteins. The specification explains how this works for multiple donors and acceptors such that a skilled artisan would understand how the invention operates. Furthermore, the detected signals are analyzed to identify one or more proteins being synthesized by producing a FRET signal from the FRET pair, computing a

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synthesis signal from the FRET signal, and interrogating a database compiled from signal data of various FRET pairs so as to identify the one or more proteins that most likely have produced the detected signals. Thus, the invention is now described in a more particular way such that this rejection is no longer applicable.

Claims 109-121 have been rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth on pages 4-6 of the office action. In response, Applicant respectfully submits that the claims have been amended to cover a preferred embodiment which is completely described and detailed in the specification such that the rejection is overcome. In particular, claim 109 recites that a first label is bound to at least one ribosome or a fragment thereof to form a donor fluorophore and that a second label is bound to at least one tRNA to form an acceptor fluorophore. Support for this language is found in the E4 data described in the specification at paragraphs [0305] to [0324]. Thus, the rejection is not applicable to the present claims.

Claims 109-121 were rejected as being unpatentable over the Odom article. The present claims have been amended to more specifically define the invention in a way that is not disclosed in or taught by Odom. As explained above, the present claims recite the binding of a first label to at least one ribosome or a fragment thereof to form a donor fluorophore; the binding of a second label to at least one tRNA to form an acceptor fluorophore; the detecting of electromagnetic radiation signals emitted when the first and second labels are in proximity due to the donor and acceptor fluorophores forming a fluorescence resonance energy transfer (FRET) pair, and the analyzing of the detected signals including the interrogating of a database compiled from signal data of various FRET pairs so as to identify the one or more proteins that most likely have produced the detected signals. This method enables the synthesis of proteins by the ribosome to be monitored in real time, *in vivo* as well as in *in-vitro*. The ribosome is engineered to carry a donor fluorophore, and tRNA and/or amino acids and/or some other part of the ribosome are either engineered to carry acceptor fluorophores. As the ribosomes mechanism processed the mRNA and tRNA molecules and synthesizes a polypeptide chain, the ribosome can be illuminated, the excite the donor fluorophores and thereby the acceptor fluorophores whenever these are in sufficient proximity to the donor fluorophores. The resulting signals are detected and used as a key for real-time database searching and identification of the protein being synthesized.

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Odom discloses the movement of tRNA during peptide bond formation on ribosomes.

Odom does not teach or suggest the presently claimed invention, either, because Odom does not disclose, teach or even suggest how monitor the synthesis of at least one protein according to the present method. The office action acknowledges that Odom does not teach the identifying sequence of the peptide, and also does not teach interrogating a database. As the claims are now directed to more specific features of these operations, the claims are now further distinguishable from Odom and the rejection should be withdrawn.

In view of the foregoing, it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated.

Respectfully submitted,

Date

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